Appendix C, attached herewith.

REMARKS

Upon entry of the above amendment, claims 3-19 and 21 will be pending in the captioned application. The claim amendments do not add new matter within the meaning of 35 U.S.C. §132. Accordingly, the Examiner is respectfully requested to enter the above amendment before examination. If the Examiner has any questions regarding this submission, she is invited to telephone the undersigned attorney.

Respectfully submitted,
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Appendix A

Claim Amendments

1. - 2. (Canceled)

3. (Currently amended) ~~Method~~ A method for preventing or reducing the onset of symptoms of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 2 (PDE2) activity is detrimental, or treating or reducing the severity of a disease in which pulmonary surfactant malfunction and/or phosphodiesterase 2 (PDE2) activity is detrimental by administering to a patient in need thereof an effective amount of (1) a pulmonary surfactant and (2) a PDE2 inhibitor.

4. (Original) The method according to claim 3, wherein an effective amount of (1) a pulmonary surfactant and (2) a PDE2 inhibitor is administered simultaneously to a patient in need thereof.

5. (Original) The method according to claim 3, wherein an effective amount of (1) a pulmonary surfactant and (2) a

PDE2 inhibitor are administered in succession, close in time or remote in time, in any order whatever to a patient in need thereof.

6. (Currently amended) ~~Use or~~ The method according to claim 3 ~~any of claims 1 to 5~~, wherein the pulmonary surfactant is selected from the group consisting of PORACTANT ALFA, BERACTANT, BOVACTANT, COLFOSCERIL PALMITATE, SURFACTANT-TA, CALFACTANT, PUMACTANT, LUSUPULTIDE and SINAPULTIDE.

7. (Currently amended) ~~Use or~~ The method according to claim 6, wherein the pulmonary surfactant is LUSUPULTIDE.

8. (Currently amended) ~~Use or~~ The method according to claim 3 ~~any of claims 1 to 5~~, wherein the PDE2 inhibitor is selected from the group consisting of N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-Benzyl-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-(3,4-Dichlorobenzyl)-9-[1-(1-

hydroxyethyl)-4-phenylbutyl]hypoxanthine, 2-(4-Fluorobenzyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 9-(1-Methyl-4-phenylbutyl)-2-[4-(3-thienyl)benzyl]hypoxanthine, 1-[5-[9-[1-(1-Hydroxyethyl)-4-phenylbutyl]hypoxanthin-2-ylmethyl]-2-methoxyphenylsulfonyl]piperidine-4-carboxylic acid, 2-(Biphenyl-4-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(4-Chlorophenyl)-9-[1-(1-hydroxyethyl)heptyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclohexyl-9-[1-(1-hydroxyethyl)-4-phenylbutyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclopropyl-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(1,3-Benzodioxol-5-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, erythro-9-(2-hydroxy-3-nonyl)adenine, 9-(6-Phenyl-2-oxohex-3-yl)-2-(3,4-dimethoxybenzyl)-purin-6-one, 6-(3,4-Dimethoxy-benzyl)-1-[1-(1-hydroxy-ethyl)-4-phenyl-butyl]-3-methyl-1,5-dihydro-pyrazolo[3,4-d]pyrimidin-4-one, N-benzyl-2-(6-fluoro-2-methyl-3-pyridin-4-ylmethylene-3H-inden-1-yl)-acetamide, (1Z)-N-benzyl-2-[6-fluoro-2-methyl-3-(3,4,5-trimethoxybenzylidene)-3H-inden-1-yl]-acetamide, N-Benzyl-2-[5-fluoro-2-methyl-1-[(Z)-(pyridin-4-yl)methylene]-1H-inden-3-yl]acetamide hydrochloride, 4-[N-[4-[9-[N-Methyl-N-(3-phenylpropyl)amino]hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid

benzyl ester, 4-[N-[4-[9-(N-hexyl-N-methylamino)hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 2-(3,4-Dimethoxybenzyl)-9-[N-methyl-N-(3-phenylpropyl)amino]hypoxanthine, 9-[N-Methyl-N-(3-phenylpropyl)amino]-2-[4-(4-methylpiperazin-1-ylsulfonyl)benzyl]hypoxanthine, 2-(3,4-Dimethoxybenzyl)-7-[1(R)-[1(R)-hydroxyethyl]-4-phenylbutyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylpentyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylhexyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 2-(3,4-Dimethoxybenzyl)-7-[1-(1-hydroxyethyl)-5-hexenyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, and the pharmaceutically acceptable salts of these compounds.

9. (Currently amended) ~~Use or~~ The method according to claim 3 ~~any of claims 1 to 8~~, wherein the PDE2 inhibitor is selected from the group consisting of N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-

(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-Benzyl-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-(3,4-Dichlorobenzyl)-9-[1-(1-hydroxyethyl)-4-phenylbutyl]hypoxanthine, 2-(4-Fluorobenzyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 9-(1-Methyl-4-phenylbutyl)-2-[4-(3-thienyl)benzyl]hypoxanthine, 1-[5-[9-[1-(1-Hydroxyethyl)-4-phenylbutyl]hypoxanthin-2-ylmethyl]-2-methoxyphenylsulfonyl]piperidine-4-carboxylic acid, 2-(Biphenyl-4-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(4-Chlorophenyl)-9-[1-(1-hydroxyethyl)heptyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclohexyl-9-[1-(1-hydroxyethyl)-4-phenylbutyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclopropyl-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(1,3-Benzodioxol-5-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, erythro-9-(2-hydroxy-3-nonyl)adenine, 9-(6-Phenyl-2-oxohex-3-yl)-2-(3,4-dimethoxybenzyl)-purin-6-one, 6-(3,4-Dimethoxy-benzyl)-1-[1-(1-hydroxy-ethyl)-4-phenyl-butyl]-3-methyl-1,5-dihydro-pyrazolo[3,4-d]pyrimidin-4-one, N-benzyl-2-(6-fluoro-2-methyl-3-pyridin-4-ylmethylene-3H-inden-1-yl)-acetamide, (1Z)-N-benzyl-2-[6-fluoro-2-methyl-3-(3,4,5-trimethoxybenzylidene)-3H-inden-1-yl]-acetamide, N-Benzyl-2-[5-fluoro-2-methyl-1-[(Z)-(pyridin-4-

yl)methylene]-1H-inden-3-yl]acetamide hydrochloride, 4-[N-[4-[9-[N-Methyl-N-(3-phenylpropyl)amino]hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 4-[N-[4-[9-(N-hexyl-N-methylamino)hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 2-(3,4-Dimethoxybenzyl)-9-[N-methyl-N-(3-phenylpropyl)amino]hypoxanthine, 9-[N-Methyl-N-(3-phenylpropyl)amino]-2-[4-(4-methylpiperazin-1-ylsulfonyl)benzyl]hypoxanthine, 2-(3,4-Dimethoxybenzyl)-7-[1(R)-[1(R)-hydroxyethyl]-4-phenylbutyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylpentyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylhexyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 2-(3,4-Dimethoxybenzyl)-7-[1-(1-hydroxyethyl)-5-hexenyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, and the pharmaceutically acceptable salts of these compounds.

10. (Currently amended) ~~Use or~~ The method according to claim 3 ~~any of claims 1 to 7~~, wherein the disease in which pulmonary surfactant malfunction and/or phosphodiesterase 2

(PDE2) activity is detrimental is ARDS or Asthma bronchiale.

11. (Currently amended) ~~Use or~~ The method according to claim 3 ~~any of claims 1 to 9~~, wherein the disease in which pulmonary surfactant malfunction and/or phosphodiesterase 2 (PDE2) activity is detrimental is selected from the group consisting of ALI, IRDS, ARDS and Asthma bronchiale.

12. (Currently amended) ~~Pharmaceutical~~ A pharmaceutical composition ~~suited for the use or method according to claims 1 to 8~~ comprising an effective amount of a pulmonary surfactant and an effective amount of a PDE2 inhibitor.

13. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 12, comprising as a fixed combination

- an effective amount of a pulmonary surfactant and
- an effective amount of a PDE2 inhibitor, and optionally
- a pharmaceutically acceptable carrier.

14. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 13, which is a fixed

pharmaceutical composition for intratracheally or intrabronchially instillation.

15. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 12, comprising as a free combination

- an effective amount of a pulmonary surfactant and optionally a pharmaceutically acceptable carrier and
- an effective amount of a PDE2 inhibitor and optionally a pharmaceutically acceptable carrier.

16. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 12 ~~any of claims 12 to 15~~, wherein the pulmonary surfactant is selected from the group consisting of PORACTANT ALFA, BERACTANT, BOVACTANT, COLFOSCERIL PALMITATE, SURFACTANT-TA, CALFACTANT, PUMACTANT, LUSUPULTIDE [[OR]] and SINAPULTIDE.

17. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 12 ~~any of claims 12 to 16~~, wherein the pulmonary surfactant is LUSUPULTIDE.

18. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 12 ~~any of claims 12 to 15~~, wherein the PDE2 inhibitor is selected from the group consisting of N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-Benzyl-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-(3,4-Dichlorobenzyl)-9-[1-(1-hydroxyethyl)-4-phenylbutyl]hypoxanthine, 2-(4-Fluorobenzyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 9-(1-Methyl-4-phenylbutyl)-2-[4-(3-thienyl)benzyl]hypoxanthine, 1-[5-[9-[1-(1-Hydroxyethyl)-4-phenylbutyl]hypoxanthin-2-ylmethyl]-2-methoxyphenylsulfonyl]piperidine-4-carboxylic acid, 2-(Biphenyl-4-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(4-Chlorophenyl)-9-[1-(1-hydroxyethyl)heptyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclohexyl-9-[1-(1-hydroxyethyl)-4-phenylbutyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclopropyl-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(1,3-Benzodioxol-5-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-

1H-purin-6-one, erythro-9-(2-hydroxy-3-nonyl)adenine, 9-(6-Phenyl-2-oxohex-3-yl)-2-(3,4-dimethoxybenzyl)-purin-6-one, 6-(3,4-Dimethoxy-benzyl)-1-[1-(1-hydroxy-ethyl)-4-phenyl-butyl]-3-methyl-1,5-dihydro-pyrazolo[3,4-d]pyrimidin-4-one, N-benzyl-2-(6-fluoro-2-methyl-3-pyridin-4-ylmethylene-3H-inden-1-yl)-acetamide, (1Z)-N-benzyl-2-[6-fluoro-2-methyl-3-(3,4,5-trimethoxybenzylidene)-3H-inden-1-yl]-acetamide, N-Benzyl-2-[5-fluoro-2-methyl-1-[(Z)-(pyridin-4-yl)methylene]-1H-inden-3-yl]acetamide hydrochloride, 4-[N-[4-[9-[N-Methyl-N-(3-phenylpropyl)amino]hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 4-[N-[4-[9-(N-hexyl-N-methylamino)hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 2-(3,4-Dimethoxybenzyl)-9-[N-methyl-N-(3-phenylpropyl)amino]hypoxanthine, 9-[N-Methyl-N-(3-phenylpropyl)amino]-2-[4-(4-methylpiperazin-1-ylsulfonyl)benzyl]hypoxanthine, 2-(3,4-Dimethoxybenzyl)-7-[1(R)-[1(R)-hydroxyethyl]-4-phenylbutyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylpentyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylhexyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 2-

(3,4-Dimethoxybenzyl)-7-[1-(1-hydroxyethyl)-5-hexenyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, and the pharmaceutically acceptable salts of these compounds.

19. (Currently amended) ~~Pharmaceutical~~ The pharmaceutical composition according to claim 12 ~~any of claims 12 to 18~~, wherein the PDE2 inhibitor is selected from the group consisting of N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, N-Benzyl-2-[5-fluoro-2-methyl-1(Z)-(3,4,5-trimethoxybenzylidene)inden-3-yl]acetamide, 2-(3'-Aminobiphenyl-4-ylmethyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-Benzyl-9-(1-methyl-4-phenylbutyl)hypoxanthine, 2-(3,4-Dichlorobenzyl)-9-[1-(1-hydroxyethyl)-4-phenylbutyl]hypoxanthine, 2-(4-Fluorobenzyl)-9-(1-methyl-4-phenylbutyl)hypoxanthine, 9-(1-Methyl-4-phenylbutyl)-2-[4-(3-thienyl)benzyl]hypoxanthine, 1-[5-[9-[1-(1-Hydroxyethyl)-4-phenylbutyl]hypoxanthin-2-ylmethyl]-2-methoxyphenylsulfonyl]piperidine-4-carboxylic acid, 2-(Biphenyl-4-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(4-Chlorophenyl)-9-[1-(1-hydroxyethyl)heptyl]-6,9-dihydro-1H-purin-6-one, 2-

Cyclohexyl-9-[1-(1-hydroxyethyl)-4-phenylbutyl]-6,9-dihydro-1H-purin-6-one, 2-Cyclopropyl-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, 2-(1,3-Benzodioxol-5-yl)-9-(1-methyl-4-phenylbutyl)-6,9-dihydro-1H-purin-6-one, erythro-9-(2-hydroxy-3-nonyl)adenine, 9-(6-Phenyl-2-oxohex-3-yl)-2-(3,4-dimethoxybenzyl)-purin-6-one, 6-(3,4-Dimethoxy-benzyl)-1-[1-(1-hydroxy-ethyl)-4-phenyl-butyl]-3-methyl-1,5-dihydro-pyrazolo[3,4-d]pyrimidin-4-one, N-benzyl-2-(6-fluoro-2-methyl-3-pyridin-4-ylmethylene-3H-inden-1-yl)-acetamide, (1Z)-N-benzyl-2-[6-fluoro-2-methyl-3-(3,4,5-trimethoxybenzylidene)-3H-inden-1-yl]-acetamide, N-Benzyl-2-[5-fluoro-2-methyl-1-[(Z)-(pyridin-4-yl)methylene]-1H-inden-3-yl]acetamide hydrochloride, 4-[N-[4-[9-[N-Methyl-N-(3-phenylpropyl)amino]hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 4-[N-[4-[9-(N-hexyl-N-methylamino)hypoxanthin-2-ylmethyl]phenyl]carbamoyl]piperidine-1-carboxylic acid benzyl ester, 2-(3,4-Dimethoxybenzyl)-9-[N-methyl-N-(3-phenylpropyl)amino]hypoxanthine, 9-[N-Methyl-N-(3-phenylpropyl)amino]-2-[4-(4-methylpiperazin-1-ylsulfonyl)benzyl]hypoxanthine, 2-(3,4-Dimethoxybenzyl)-7-[1(R)-[1(R)-hydroxyethyl]-4-phenylbutyl]-5-

methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylpentyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 7-(1-Acetylhexyl)-5-methyl-2-(4-methylbenzyl)imidazo[5,1-f][1,2,4]triazin-4(3H)-one, 2-(3,4-Dimethoxybenzyl)-7-[1-(1-hydroxyethyl)-5-hexenyl]-5-methylimidazo[5,1-f][1,2,4]triazin-4(3H)-one, and the pharmaceutically acceptable salts of these compounds.

20. (Canceled)

21. (Currently amended) ~~Method~~ A method for preparing a pharmaceutical composition of claim 12 ~~the claims 12 to 14~~ comprising the step: mixing an effective amount of a pulmonary surfactant and a PDE2 inhibitor with a pharmaceutically acceptable carrier.